

A composition comprising a compound of formula (I) or (II):

5 wherein

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A₁ is $-C(J_1)=$, or -N=;

A2 is $-C(J_1)_2$, $-N(J_1)$, $-N(O)(J_1)$, -N(O)=, -S, -S(O), $-S(O)_2$ or -O;

 E_1 is $-(CR_1R_1)_{m_1}W_1$;

 G_1 is N_3 , -CN, -OH, -OR_{6a}, -NO₂, or -(CR₁R₁)_{m1}W₂;

10 T₁ is -NR₁W₃, a heterocycle, or is taken together with U₁ or G₁ to form a group having the structure



U₁ is H or -X₁W₆;

J1 and J1a are independently R1, Br, Cl, F, I, CN, NO2 or N3;

J₂ and J_{2a} are independently H or R₁;

R₁ is independently H or alkyl of 1 to 12 carbon atoms;

R₂ is independently R₃ or R₄ wherein each R₄ is independently substituted with 0 to 3 R₃ groups;

R₃ is independently f, Cl, Br, I, -CN, N₃, -NO₂, -OR_{6a}, -OR₁, -N(R₁)₂,

20 $-N(R_1)(R_{6b})$, $-N(R_{6b})_2$, $-SR_1$, $-SR_{6a}$, $-S(O)R_1$, $-S(O)_2R_1$, $-S(O)OR_1$, $-S(O)OR_{6a}$,

 $-S(O)_2OR_1$, $-S(O)_2OR_{6a}$, $-C(O)OR_1$, $-C(O)R_{6c}$, $-C(O)OR_{6a}$, $-OC(O)R_1$,

 $-N(R_1)(C(O)R_1)$, $-N(R_{6b})(C(O)R_1)$, $-N(R_1)(C(O)OR_1)$, $-N(R_{6b})(C(O)OR_1)$,

 $-C(O)N(R_1)_2$, $-C(O)N(R_{6b})(R_1)$, $-C(O)N(R_{6b})_2$, $-C(NR_1)(N(R_1)_2)$,

 $-C(N(R_{6b}))(N(R_1)_2)$, $-C(N(R_{1}))(N(R_1)(R_{6b}))$, $-C(N(R_{6b}))(N(R_1)(R_{6b}))$,

25 $-C(N(R_1))(N(R_{6b})_2)$, $-C(N(R_{6b}))(N(R_{6b})_2)$, $-N(R_1)C(N(R_1))(N(R_1)_2)$,

 $-N(R_1)C(N(R_1))(N(R_1)(R_{6b})), -N(R_1)C(N(R_{6b}))(N(R_1)_2),$

 $-N(R_{6b})C(N(R_1))(N(R_1)_2)$, $-N(R_{6b})C(N(R_{6b}))(N(R_1)_2)$,

 $-N(R_{6b})C(N(R_1))(N(R_1)(R_{6b})), -N(R_1)C(N(R_{6b}))(N(R_1)(R_{6b})),$

 $-N(R_1)C(N(R_1))(N(R_{6b})_2)$, $-N(R_{6b})C(N(R_{6b}))(N(R_1)(R_{6b}))$,

 $-N(R_{6b})C(N(R_1))(N(R_{6b})_2)$, $-N(R_1)C(N(R_{6b}))(N(R_{6b})_2)$, $-N(R_{6b})C(N(R_{6b}))(N(R_{6b})_2) = 0$, =S, $=N(R_1)$ or $=N(R_{6b})$; R4 is independently alkyl of 1 to/12 carbon atoms, alkenyl of 2 to 12 carbon atoms, or alkynyl of 2 to 12 carbon atoms; R5 is independently R4 wherein each R4 is substituted with 0 to 3 R3 groups; R5a is independently alkylene of 1 to 12 carbon atoms, alkenylene of 2 to 12 carbon atoms, or alkynyleng of 2-12 carbon atoms any one of which alkylene, alkenylene or alkynylene is substituted with 0-3 R3 groups; R_{6a} is independently H ϕ r a protecting group for hydroxyl or thio; R_{6b} is independently H, a protecting group for amino or the residue of a carboxyl-containing compound; R_{6c} is independently H or the residue of an amino-containing compound; W1 is a group comprising an acidic hydrogen, a protected acidic group, or an R₆c amide of the group comprising an acidic hydrogen; W2 is a group complising a basic heteroatom or a protected basic heteroatom, or an R6b amide of the basic heteroatom; W3 is W4 or W5; W4 is R5 or -Q(O)R -Q(O)W5, $-SO_2R5$, or $-SO_2W5$; W5 is carbocycle of heterocycle wherein W5 is independently substituted with 0 to 3 Rz groups; W6 is -R5, -W $\frac{1}{5}$, -R5aW $\frac{1}{5}$, -C(O)OR6a, -C(O)R6c, -C(O)N(R6b)2, $-C(NR_{6b})(N(R_{6b})_2)$, $-C(NR_{6b})(N(H)(R_{6b}))$, $-C(N(H)(N(R_{6b})_2)$, $-C(S)N(R_{6b})_2$, or -C(O)R₂; X_1 is a bond, -O-, -N(H)-, - $N(R_5)$ -, -N(OH)-, - $N(OR_5)$ -, - $N(NH_2)$ -, $-N(N(H)(R_5))$ -, $-N(N(R_5)^{\frac{1}{2}})$ -, $-N(H)N(R_5)$ -, -S-, -SO-, or -SO₂-; and each m1 is independently an integer from 0 to 2; provided, however, that dompounds are excluded wherein: A₁ is CH = or -N = and A₂ is -CH₂-;(a) (b) E₁ is COOH, P(O)(OH)₂, SOOH, SO₃H, or tetrazol; (c) G₁ is $(N, N(H)R_{20}, N_3, SR_{20}, OR_{20}, guanidino,$ OR₂₀

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- (d) T_1 is -NHR₂₀;
- (e) R20 is H; an acyl group having 1 to 4 carbon atoms; a linear or cyclic alkyl group having 1 to 6 carbon atoms, or a halogen-substituted analogue thereof; an allyl group or an unsubstituted aryl group or an aryl substituted by a halogen, an OH group, an NO2 group, an NH2 group or a COOH group;
- (f) J_1 is H and J_{1a} is H, F C_1 , Br or CN;
- (g) J_2 is H and J_{2a} is H, CN or N_3 ;
- (h) U₁ is CH₂YR_{20a}, CH₂YR_{20a}CH₂YR_{20a} or CH₂YR_{20a}CH₂YR_{20a};
- (i) R_{20a} is H-or acyl having 1 to 4 carbon atoms;
- (j) Y is O,/S,\H\o,r N,H;
- (k) 0 to $2/YR_{20/2}$ are H, and
- (l) successive Y moieties in a U₁ group are the same or different, and when Y is H then R_{20a} is a covalent bond, and the pharmaceutically acceptable salts and solvates thereof;

and the salts, solvates resolved enantiomers and purified diastereomers thereof.

- 2. A method of inhibiting the activity of neuraminidase comprising the step of contacting a sample suspected of containing neuraminidase with the composition of Claim 1.
- A method of treatment or prophylaxis of influenza virus infection in a host comprising administration to the host, by a route other than topically to the respiratory tract, of a therapeutically effective dose of an antivirally active compound of the formula:

$$R^{5}_{m}$$
 A R^{1} R^{2} R^{3} R^{3} R^{3} R^{3} R^{3} R^{2} R^{3} R^{3} R^{3}

wherein:

in general formula (x), A is oxygen, carbon or sulphur, and in general formula (y), A is nitrogen or/carbon;

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R¹ denotes COOH, P(O)(OH)₂, NO₂, SOOH, SO₃H, tetrazol, CH₂CHO, CHO or CH(CHO)₂,

R² denotes H, OR⁶, F, Cl, Br, CN, NHR⁶, SR⁶, or CH₂X, wherein X is NHR⁶, halogen or OR⁶ and

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R⁶ is hydrogen; an acyl group having 1 to 4 carbon atoms; a linear or cyclic alkyl group having 1 to 6 carbon atoms, or a halogen-substituted analogue thereof; an allyl group or an unsubstituted aryl group or an aryl substituted by a halogen, an OH group, an NO₂ group, an NH₂ group or a COOH group,

R³ and R³ are the same or different, and each denotes hydrogen, CN, NHR⁶, N₃, SR⁶, =N-OR⁶, OR⁶, guanidino,

$$N-R^6$$
, NR^6 , $N \rightarrow O$, $NH\cdot N-R^6$
 $NH\cdot$

R⁴ denotes NHR⁶, SR⁶, OR⁶, COOR⁶/NO₂, C(R⁶)₃, CH₂COOR⁶, CH₂NO₂ or CH₂NHR⁶, and

R⁵ denotes CH₂YR⁶, CHYR⁶CH₂YR⁶ or CHYR⁶CHYR⁶CH₂YR⁶, where Y is O, S, NH or H, and successive Y mojeties in an R⁵ group are the same or different,

and pharmaceutically acceptable salts or derivatives thereof, provided that in general formula (x)

- (i) when R³ or R³ is OR⁶ or hydrogen, and A is oxygen or sulphur, then said compound cannot have both
 - (a) an R² that is hydrogen and
 - (b) an R4 that is NH-acyl, and
- (ii) R⁶ represents a covalent bond when Y is hydrogen, and that in general formula (y),
- (i) when R³ or R³' is OR⁶ or hydrogen, and A is nitrogen, then said compound cannot have both
 - (a) an R² that is hydrogen, and
 - (b) an R4 that is NH-acyl, and
 - (ii) R⁶ represents a covalent bond when Y is hydrogen.

- 4. The composition of Claim 1 where further excluded are compounds wherein G₁ is -N(R₂₁)C(=N(R₂₁))N(R₂₁)₂ and R₂₁ is independently H, C₁-C₆ alkyl, C₃-C₈ cycloalkyl, C₁-C₆ alkoxy, aryl, aralkyl, aryloxy, aralkyloxy, amino, hydroxy, cyano, nitro, COR₂₂, CO₂R₂₂, SO₂R₂₂ (where R₂₂ is C₁-C₆ alkyl or aralkyl), or CONR₂₃ (where R₂₃ is independently H or C₁-C₆ alkyl or aralkyl).
- 5. The composition of claim 1 wherein X₁ is a bond and W₆ is neither C₁-C₃ normal alkyl nor C₁-C₃ normal alkyl substituted with 1 to 3 OH, SH or NH₂.
- 6. The composition of claim 1 wherein X1 is a bond and W6 is neither C1-C3 normal alkyl nor C1-C3 normal alkyl substituted with 1 to 3 OH, SH or NH2.
- 7. The composition of claim 1 wherein X₁ is a bond and W₆ is neither C₁-C₃ normal alkyl nor C₁-C₃ normal alkyl substituted with 1 to 3 OH, OR_{6a}, SH or NH₂, wherein this R_{6a} is a protecting group.
- 20 8. The composition of claim 1 wherein X1 is a bond and W6 is neither C1-C3 normal alkyl nor C1/C3 normal alkyl substituted with 1 to 3 OH, OR6a, SH or NH2, wherein this R6a is a protecting group.
- 9. The composition of claim 1 wherein the proviso further excludes compounds wherein G₁ is (alk)_{m4}NR^{6b}R^{7b};

alk is unsubstituted or substituted methylene;

m₄ is 0 or 1;

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R^{6b} is hydrogen, C₁₋₆alkyl, aryl, araalkyl, amidine, NR^{7b}R^{8b}, or an unsaturated or saturated ring containing one or more heteroatoms;

R^{7b} is hydrogen, C₁₋₆alkyl, or allyl, or NR^{6b}R^{7b} forms an optionally substituted 5 or 6 membered ring optionally containing one or more additional heteroatoms; and

R^{8b} is hydrogen or C₁-6alkyl.

35 10. The composition of claim 9 wherein the proviso further excludes compounds wherein G₁ is NR^{6b}R^{7b}.

- 11. The composition of claim 1 wherein W_6 is C_1 - C_3 alkyl substituted with 1 to 3 OR_{6a} or SR_{6a} , which OR_{6a} or SR_{6a} groups are stable to hydrolysis in gastrointestinal fluid.
- 5 12. The composition of claim 1 wherein if W₆ is substituted with R₃ and R₃ is substituted with OR_{6a} then this R_{6a} is not acetyl.
 - 13. The composition of claim 1 wherein W_6 is -(CH2)_{m1}CH((CH2)_{m3}R3)2, -(CH2)_{m1}C((CH2)_{m3}R3)3; -(CH2)_{m1}CH((CH2)_{m3}R5_aW5)2;
- 10 $-(CH_2)_{m1}CH((CH_2)_{m3}R_3)((CH_2)_{m3}R_5 W_5);$ $-(CH_2)_{m1}C((CH_2)_{m3}R_3)_2(CH_2)_{m3}R_5 W_5), (CH_2)_{m1}C((CH_2)_{m3}R_5 W_5)_3 or$ $-(CH_2)_{m1}C((CH_2)_{m3}R_3)((CH_2)_{m3}R_5 W_5)_2 and m_3 is an integer from 1 to 3.$
- 14. The composition of Claim-1, wherein X₁ is a bond and W₆ is -R₅, -W₅ or -R_{5a}W₅.
 - 15. The composition of Claim $\frac{1}{2}$ having Formula (I) wherein A₁ is -C(J₁)=, X₁ is a bond and W₆ is R₅.
- 20 16. The composition of Claim 15 wherein said R5 is R4 substituted with 0 to 3 -OR1.
 - 17. The composition of Claim 15 wherein said R5 is R4 substituted with 0 to 3 -NO2 or N3 groups.
 - 18. The composition of Claim 16 wherein said -OR1 is present and at least one of said R1 is C4-C12.
 - 19. The composition of ψ laim 1 wherein U₁ is -N(R₅)₂, -N(H)(CH(R₅b)₂),
- 30 -N(H)(CH₂CH(R_{5c})₂), -N(ϕ R₅)(R₅), -N(N(H)(R₅))(R₅), -N(H)(N(R₅)₂),
 - $-N(R_5)(C(O)R_5)$, $-C(O)N(R_5)_2$, $-C(S)N(R_5)_2$, $-OR_{5d}$, $-OCH(R_{5b})_2$,
 - $-OCH_2CH(R_{5c})_2$, $-SR_{5d}$, $-SCH(R_{5b})_2$, $-SCH_2CH(R_{5c})_2$, $-S(O)R_{5d}$,
 - -S(O)CH(R_{5b})₂, -S(O)CH₂CH(R_{5c})₂, -S(O)₂R_{5d}, -S(O)₂CH(R_{5b})₂,
 - $-S(O)_2CH_2CH(R_{5c})_2$, $-C(N(R_5))(N(H)(R_5))$, $-C(O)R_{5d}$, $-C(O)CH(R_{5b})_2$ or
- 35 -C(O)CH2CH(R5c)2; and

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wherein:

hydrogen of said U₁ -CH₂- or -CH- moieties optionally is substituted with -OR₁, -\$R₁, NO₂, N₃, F, -CN, Cl or Br;

R5b is independently alkyl of 1 to 11 carbon atoms, alkenyl of 2 to

11 carbon atoms or alkynyl of 2 to 11 carbon atoms any one of which alkyl, alkenyl or alkynyl groups is substituted with 0 - 3 R3 groups;

R5c is independently alkyl of 1 to 10 carbon atoms, alkenyl of 2 to 10 carbon atoms or alkynyl of 2 to 10 carbon atoms any one of which alkyl, alkenyl or alkynyl groups/is substituted with 0 - 3 R3 groups;

R5d is a branched R5 group; and

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wherein if R5, R5c or R5d is substituted with 1 - 3 R3 groups then R3 is -OR1, -SR1, NO2, N3, F, -CN, Cl or Br.

10 20. The composition of claim 1 having Formula (I) wherein A₁ is -C(J₁)=, and W₆ is a branched chain R₄ group of 3 to 8 carbon atoms.